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Optimal Number of Endoscopic Biopsies in Diagnosis of Advanced Gastric and Colorectal Cancer

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Endoscopic biopsy is necessary to confirm a histopathologic diagnosis. Currently, 6 to 8 biopsies are recommended for diagnosis of a suspected malignant lesion. However, multiple biopsies may result in several problems, such as an increased risk of bleeding, procedure prolongation, and increased workload to pathologists. The aim of this study was to clarify the optimal number of endoscopic biopsy specimens required in diagnosis of advanced gastrointestinal cancer. Patients who were diagnosed with advanced gastrointestinal cancer during endoscopy were included. Five specimens were obtained sequentially from viable tissue of the cancer margin. Experienced pathologists evaluated each specimen and provided diagnoses. A total of 91 patients were enrolled. Fifty-nine subjects had advanced gastric cancer, and 32 had advanced colon cancer. Positive diagnosis rates of the first, second, and third advanced gastric cancer specimens were 81.3%, 94.9%, and 98.3%, respectively, while positive diagnosis rates of advanced colon cancer specimens were 78.1%, 87.5%, and 93.8%. Further biopsies did not increase positive diagnosis cumulative rates. This study demonstrated that three specimens were sufficient to make correct pathologic diagnoses in advanced gastrointestinal cancer. Therefore, we recommend 3 or 4 biopsies from viable tissue in advanced gastrointestinal cancer to make a pathologic diagnosis during endoscopy.

Key Words: Endoscopy, Gastrointestinal; Biopsy; Stomach Neoplasms; Colonic Neoplasms

INTRODUCTION

Since fiberscope was introduced in 1958, gastroscopy and colonoscopy have made large contributions in the diagnosis of gastrointestinal disease; additionally, the development of the video endoscope provided further diagnostic improvement (1, 2). During endoscopy, multiple biopsies are often necessary to diagnose cancer at the potential malignant lesion site in the stomach or colon as a standard diagnostic tool for pathologic confirmation. Twenty to thirty years ago, the number of endoscopic biopsy specimens needed to diagnose gastric or colon cancer during fiberoptic endoscopy varied from 4 to 10 (3-6). However, the increase in the number of biopsies performed may cause an increased risk of complications, such as gastrointestinal bleeding. Only a few recent reports have been published on the optimal number of endoscopic biopsy specimens required to correctly diagnose gastric or colon cancer. Currently, we can routinely differentiate malignant from benign lesions according to the endoscopic finding. Furthermore, with the development of the video-endoscope instrument, we could get a wider vision, and better targeting to the suspicious lesion, that leads to a reduced number of biopsy specimens needed to diagnose malignancy. The aim of this study was to clarify the optimal number of endoscopic biopsy specimens in lesions suspected as advanced gastric and colon cancer.

MATERIALS AND METHODS

A total of 91 patients who underwent diagnostic gastroscopy and colonoscopy for various gastrointestinal symptoms at the Kangbuk Samsung Hospital from January 2006 to May 2007 was included in this study. All patients enrolled in this study were diagnosed with advanced gastric or colon cancer by endoscopy which was subsequently confirmed by surgical pathologic diagnosis. Upper endoscopic examinations were performed using forward viewing standard electronic video gastroscopes (EC-450WR5; Fujinon Co. Ltd., Saitama, Japan) between 8:00 a.m. and 12:00 a.m. after an overnight fast. Colonoscopy was performed using standard electronic video colonoscopes (EC-450WM5; Fujinon Co. Ltd.) between 2:00 p.m. and 5:00 p.m. after an overnight fast. Bowel preparation was accomplished by instructing patients to drink 4 L of a polyethylene glycol-electrolyte solution (Colonlyte®; Taejun Co., Seoul, Korea) from 6:00 a.m. to 10:00 a.m.

During the endoscopic examination, 5 biopsy specimens were

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taken from suspected lesion using standard biopsy forceps. Biopsy specimens were obtained from the inner margin of ulcer in all directions. Each biopsy specimen was immediately immersed (fixed) in 20% formalin solution in separate vials; each vial was given a code number to identify the serial order. One expert pathologist who was not aware of the code numbers made the diagnosis of each biopsy specimen. The diagnoses used for single biopsy were one of the following: 1) carcinoma, 2) presumable carcinoma, 3) benign biopsy, and 4) failed biopsy. In the case of 1) or 2), the final diagnosis was considered to be carcinoma.

Location, size, shape, and macroscopic classifications of the lesion suspected of malignancy were recorded immediately after the procedure by endoscopists. Patient's age, sex, and principal symptoms, and the reason why the patient underwent diagnostic endoscopy were recorded after the procedure by nurses in endoscopy room. The data were collected prospectively. Reports of pathologic results were reviewed retrospectively, and before data analysis, pathologic results were reviewed again retrospectively.

The data obtained during this study were expressed as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. For analyzing cumulative diagnostic yields of pathology according to the order of endoscopic biopsy specimens, nonparametric Cochrane and McNemar tests were used. Statistical significance was accepted for $P < 0.05$. All analyses were conducted using SPSS version 13.0 (SPSS Inc, Chicago, IL, USA).

Table 1. Location of advanced gastric cancer (AGC) and colon cancer (ACC)

Cancer	Location	No. (%)
AGC	Antrum	28 (47.4)
	Angle	3 (5.1)
	Body	
	Lower	6 (10.2)
	Middle	14 (23.7)
	Upper	5 (8.5)
	Cardia	3 (5.1)
ACC	Cecum	1 (3.1)
	Ascending colon	2 (6.2)
	Transverse colon	3 (9.4)
	Descending colon	1 (3.1)
	Sigmoid colon	17 (53.1)
	Rectum	8 (25.0)

Ethical statement

This study protocol was approved by the institutional review board of Kangbuk Samsung Hospital (Approval number: KBC-11125). Written informed consent was exempted, and all data collected from this study were kept confidential.

RESULTS

A total of 91 patients with 59 advanced gastric and 32 colorectal cancers were enrolled. There was no significant difference in age and gender (Age: 60.3 ± 13.2 yr in gastric cancer patients vs 62.0 ± 14.1 yr in colon cancer patients). The male to female ratio was 2.68 in gastric cancer patients and 2.2 in colon cancer patients. Frequent sites of advanced gastric cancer were the antrum (47.4 %) and body (42.4%), and those of colon cancer were the sigmoid colon (53.1%) and rectum (25.0%) as shown in Table 1.

In macroscopic and pathologic classifications, Borrmann type 3 (n = 36, 61.0%) and tubular-adenocarcinoma (n = 47, 79.7%) were most frequently reported in advanced gastric cancer and Borrmann type 3 (n = 15, 46.9%) and tubular-adenocarcinoma (n = 28, 87.5%) were most frequently reported in advanced colon cancer (Table 2, 3).

Examination of the diagnostic yield of pathology according to the number of endoscopic biopsy specimens showed that initial biopsies had a diagnostic accuracy of 81.3% in advanced gastric cancer and 78.1% in advanced colon cancer.

Cumulative rates of diagnostic accuracy from the first to second biopsy, the first to third, and the first to fourth were 94.9%, 98.3%, and 98.3%, respectively, in advanced gastric cancer, whereas the rates were 87.5%, 93.8%, and 98.3% in advanced colon cancer (Fig. 1). Further additional biopsies did not show any additional benefit in diagnostic rates. Only one case of gas-

Table 2. Macroscopic classification of advanced gastric and colorectal cancer

Cancer	Borrmann type			
	1	2	3	4
AGC No. (%)	3 (5.1)	16 (27.1)	36 (61.0)	4 (6.8)
ACC No. (%)	3 (9.4)	14 (43.7)	15 (46.9)	0 (0)

AGC, advanced gastric cancer; ACC, advanced colon cancer.

Table 3. Pathology of advanced gastric and colorectal cancer

Cancer	Pathology					
	Tubular-adenocarcinoma			Mucinous adenocarcinoma	Signet ring cell cancer	Others
	Well differentiated	Moderately differentiated	Poorly differentiated			
AGC No. (%)	5 (8.5)	47 (79.7) 21 (35.6)	21 (35.6)	2 (3.4)	8 (13.5)	2 (3.4)
ACC No. (%)	4 (12.5)	28 (87.5) 22 (68.7)	2 (6.2)	1 (3.1)	1 (3.1)	2 (6.2)

Histology of advanced gastric and colorectal cancer was classified in accordance with WHO classification. AGC, advanced gastric cancer; ACC, advanced colon cancer.

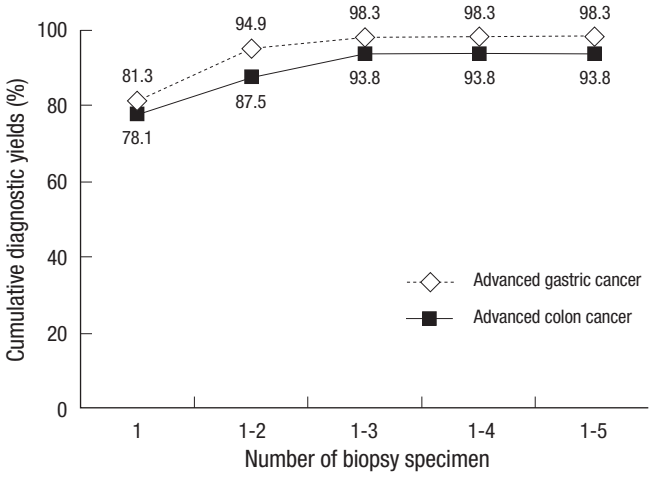

Fig. 1. Cumulative diagnostic yield according to the order of endoscopic biopsy specimens in advanced gastric cancer and colon cancer.

tric cancer and two cases of colon cancer were non-diagnostic with five biopsy specimens.

DISCUSSION

Until recently, it was believed that multiple biopsies can increase pathologic diagnosis rates of gastric or colon cancer during endoscopic examination. However, this study showed that the number of biopsies needed to diagnose malignant cells during endoscopy could be reduced to three or four.

Several studies have been published about factors that influence biopsy results in gastrointestinal malignancy diagnoses. In one study, diagnostic accuracy improved with an increase in the number of biopsy specimens and reached 100% when 6 or more biopsy specimens were obtained (7). In another study, it was recommended that at least 10 biopsy specimens should be taken from suspected malignant gastric lesions, and the overall endoscopic biopsy accuracy was 99.8% (8). Others found that when eight specimens were taken, greater than 99% chance of correct tissue diagnosis in gastrointestinal cancer during endoscopy was seen (4). However, all these reports were published 30 yr ago. In a report published 20 yr ago, if two biopsy specimens were taken, the correct diagnosis was achieved in 95.8% of cases, and that rate increased to 97.9% and 100% if 4 or 6 specimens were taken, respectively, in esophageal cancers (6). In the case of gastric cancers, 97% accuracy could be achieved when 5 biopsy specimens were taken (3). In a recent study of missed diagnosis in patients with upper gastrointestinal cancers, 77% of patients had fewer than 4 biopsy samples taken at previous endoscopies, compared with 37% at the final endoscopy (9). However, a thorough analysis in that study revealed that in only one case was insufficient number of biopsy samples taken, from a total of 16 cases. Additionally, the number of biopsy specimens and gross endoscopic shapes of lesions were not described. Therefore, the reason for the missed diagnoses is not clear in that report.

Actually, all the number of biopsy specimens is not the most important factor in the diagnosis of gastric cancer during endoscopy; the acquisition of appropriate tissue from the lesion with exact targeting is more important. Advance in endoscopic instrumentation have led to electronic rather than fiber-optic scopes, and the shaft is more flexible. Endoscopic vision has improved, the visual field is wider, and the scope can access inner portions that were unviewable in the past. Biopsy forceps also evolved and became more delicate and able to punch adequate amount of tissues. Such progresses make it easier to target suspicious lesions for biopsy during endoscopy and reduce the number of biopsy specimens for tissue diagnosis.

The biopsy site is also important. In a previous study, tissue obtained from the rim of an ulcer showed more accurate diagnostic results compared to those taken from ulcer base because insufficient tissue structure consisting of only necrotic debris and exudates may be present in ulcer base (5, 7, 10). Taking biopsy specimens from ulcer base has also has a higher risk of bleeding due to exposed submucosal vessels within ulcer base. In our study, the diagnostic accuracy from ulcer base was also lower than that from the inner margin. Therefore, targeting of an appropriate site is very important and especially targeting of first a few biopsies is more important, especially if taking multiple specimens from the same site, as the endoscopic visual field might be impaired after the first biopsy. The biopsy itself can transform original shape of the target lesion, and bleeding by the initial biopsy can cover the lesion and result in poor peripheral vision. If a former biopsy has performed, it may also be more difficult to obtain correct specimen.

Along the increase in the number of endoscopic examinations, experiences of gastroscopy or colonoscopy and knowledge about endoscopic lesions have been accumulating. In addition to their own personal experiences, endoscopists have learned about many other cases from books, journals, graduate or continuing medical education at conferences, and even via Internet. Therefore, experienced endoscopists can differentiate malignant lesions from benign lesions by examination of its gross appearance and need not take excessive number of biopsies.

Pathologists also become experts with their growing knowledge and experience in the gastrointestinal department. In large centers, gastrointestinal pathology specialists are available to give their expert opinions and help with diagnosis in difficult cases. There have been many developments in histological diagnosis as well. Many kinds of special stains have been introduced and are now utilized in clinical practice. Therefore, pathologic diagnosis does not depend on only H & E staining, and pathologists can make diagnoses by other complementary special staining with the same biopsy specimens.

In our study, there was only one case in which malignant cells were not found in any of the gastroscopic biopsies, even a sub-

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sequent seventh biopsy. It was a case of advanced gastric cancer of Borrmann type 4. Due to its peculiar biological properties, in which a submucosal spread of malignant cells was present without a mucosal lesion, malignant cells could not be obtained by subsequent repeated endoscopic biopsy. A second endoscopy for re-biopsy a few days later also failed to give us malignant cells. In this case, we could diagnose malignancy with radiologic studies, and pathologic diagnosis was confirmed after surgery.

Among the colon cancers surveyed in this study, two cases were not diagnosed by endoscopic biopsy preoperatively. In these cases, because of luminal obstruction by the cancer mass, exact targeting with biopsy forceps was not possible. In contrast to the stomach, lumen of the colon is not wide, and retroflection of the scope is not possible. Thus, targeting accuracy in colon cancer is lower than that in the stomach. They underwent surgery with an impression of malignant stenosis to relieve obstruction and also pathologically diagnosed after surgery.

In summary, the diagnostic accuracy of endoscopic biopsy for advanced gastric or colon malignancy is increased according to the number of biopsies performed, up to the third biopsy. Further biopsies do not increase rates of correct diagnosis. Additional biopsies may increase the workload of both endoscopists and pathologists. The collection of multiple specimens also prolongs endoscopic procedure and provokes more discomfort to the patient. Furthermore, an increase in the number of biopsies will increase the risk of bleeding from the biopsy site. Therefore, we recommend 3 or 4 biopsy specimens from one viable tissue for pathologic diagnosis of advanced gastrointestinal malignancy during endoscopy. In cases of negative results with the endoscopic impression of malignancy, re-biopsy with careful targeting should be performed.

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